
BIOGRAPHICAL SKETCH

NAME: **Holly A. Ingraham, Ph.D.**

eRA COMMONS USER NAME (credential, e.g., agency login): **hollyi**

POSITION TITLE: **Professor of Cellular and Molecular Pharmacology, UCSF**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of California, San Diego (Revelle College)	B.A.	1975	Biology-High Honors
University of California, San Diego (Revelle College)	B.A.	1975	Psychology-High Honors
University of California, San Diego	Ph.D.	1981	Physiology/Pharmacology

A. Personal Statement

We study hormonal control of neuronal circuits in the female brain and peripheral tissues. We are particularly keen to understand how fluctuations or permanent loss of estrogen during different life stages trigger **adaptive responses specific to female physiology**. Defining the cellular and molecular basis of hormone action in estrogen-responsive neurons and cells is highly relevant to chronic disorders that degrade the quality of life for women of all ages. Among the multiple sex-biased diseases affecting women, our work is highly relevant to age-related metabolic decline, irritable bowel syndrome, endometriosis, and osteoporosis. My initial research program at UCSF defined molecular pathways controlling the early phases of mammalian sex determination. Today, we continue to study sex differences in the gut and brain. As evidenced by our publication record, we engage in multi-faceted approaches that span neuroscience, mouse genetics, and whole animal physiology. Recent publications are listed below.

1. Babey ME, Krause WC, Chen K, Herber CB, Torok, Z., Nikkanen J, Rodriguez R, Zhang X, Castro-Navarro F, Wang Y, Villeda S, Wheeler, Leach, JK, Lane NE, Scheller EL, Chan CKF, Ambrosi TH, and **H.A. Ingraham**. A Maternal Brain Hormone that Builds Bone. [BioRxiv](#) (2023) Aug 29; PubMed PMID: 37693376; PMCID: PMC10491109, [Nature](#) (2024) AOP July 10th, PMID: 38987585.
2. Nikkanen, J. Leong, Y.A, Krause W.C., Corbit K.C., Tran J.L., Dermadi D., Masche, J.A., Van Ry T., Cox J.E., Weiss E.J., Gokcumen, O., Chawla, A., and **H.A. Ingraham**. An evolutionary trade-off between host immunity and metabolism drives fatty liver in male mice. [Science](#) (2022) Oct 21;378(6617):290-295, PMID: 36264814.
3. *Bayrer, J.R., Castro, J., Venkataraman, A., Touhara, K.K., Rossen, N.D., Morrie, R.D., Hendry, Madden, A.J., Braverman, K.N., Schober. G., Brizuela, M., Castro-Navarro, F., Bueno-Silva, C., ***Ingraham, H.A.**, *Brierley, S.M. and D. Julius. Gut Enterochromaffin Cells are Critical Drivers of Visceral Pain and Anxiety [Nature](#) (2023) Mar;616 (7955): 137-142 ***Co-corresponding Author**.

New Research Briefing: **Ingraham, H.A.** and S.M. Brierley. Specialized gut cells coupled with nerves contribute to the sex bias of gut pain, [Nature Portfolio](#), 2023.

4. Krause, W.C., R. Rodriguez, B. Gegenhuber, N. Matharu, A.N. Rodriguez, A.M. Padilla, K. Toma, C.B. Herber, S.M. Correa, X. Duan, N. Ahituv, J. Tollkuhn, and **H.A. Ingraham**. Oestrogen engages brain MC4R signaling to drive physical activity in female mice. [Nature](#) (2021) Nov;599(7883):131-135. Epub 2021 Oct 13, PMID:34646010.

Another primary focus of my academic activities is aimed at enhancing our nation's biomedical educational pipeline. I serve as the **Director of the UCSF NIGMS-IRACDA program**, which is highly successful, placing ~65% of Scholars in faculty positions at R1/R3 institutes; the UCSF program was recently renewed in 2023 for five years. Funding provides a cohort of 12 postdoctoral scholars with individualized mentoring and career development plans, including assisting them with NIH K transition awards and faculty job applications. A recent Q&A session published in the November issue of [Neuron](#) highlights my reflections on my career path as a senior female scientist in biomedical research and the need to push more basic research in women's health.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

- 2020 – Pres. Herzstein Endowed Professor of Molecular Physiology
2016 – Pres. Director of UCSF IRACDA Scholar Program to Promote Diversity
2010 – 2020 Associate Vice-Chair, UCSF, Dept. of Cellular and Molecular Pharmacology
2004 – Pres. Professor, UCSF, Dept. Cellular and Molecular Pharmacology
2004 – Pres. Herzstein Distinguished Investigator in Molecular Physiology
2002 – 2007 Professor, UCSF, Department of Physiology with a joint appointment in the Department of OB/GYN and Reproductive Sciences
1999 – 2002 Associate Professor, UCSF, Department of Physiology with a joint appointment in the Department of Reproductive Sciences
1994 – 1999 Assistant Professor, Tenure Track UCSF, Department of Physiology with a joint appointment in the Department of Reproductive Sciences
1991 – 1994 Assistant Professor in Residence, with Joint appointment in the Department of Physiology University of California, San Francisco, and OB/GYN and Reproductive Sciences
1990 – 1991 Assistant Research Endocrinologist, Dept. of Medicine, University of California, San Diego
1987 – 1990 Research Associate with Dr. Michael Geoffrey Rosenfeld HHMI, University of California, San Diego
1981 – 1985 Postdoctoral Fellow and Research Associate with Drs. G.A. Evans and S.F. Heinemann, The Salk Institute for Biological Studies
1977 – 1981 Physiology and Pharmacology Graduate Student with Dr. M. Goulian, University of California, San Diego, Dept. of Medicine. Thesis "Effects of 5-Fluorodeoxyuridine on intracellular metabolism of deoxyuridylate."

Awards and Honors

- 2026 Harris Memorial Lectureship – International Congress of Neuroendocrinology, Nagoya, JAPAN
2025 Keynote Lecture, Cedars Sinai Women's Health Research, Los Angeles, CA
2025 Dolan Pritchett Honorary Lecture, Perlman School of Medicine, U. of Penn, Philadelphia, PA
2024 Keynote Lecture 1st Intl Conference on Steroid Hormones and Receptors, Albuquerque, NM
2024 Wu Lectureship, Institute for Human Nutrition, New York, NY
2024 **FASEB Excellence in Science Lifetime Achievement Award** (Keynote @ 2025 APS Summit)
2024 Keynote Lecture Women's History Month Symposium, UC Davis, Davis, CA
2023 **UCSF Lifetime Achievement in Mentoring Award**
2023 Marlene A. DeLuca Endowed Lectureship, UCSF, San Diego, CA
2023 Society of Endocrinology Trans-Atlantic Medalist and Lecture, Glasgow, UK
2023 Women in Medicine and Science (WIMS) Lectureship, U. of Arizona, Tucson, AZ
2023 Edwin B. Astwood Award for Outstanding Research in Basic Science, Endocrine Society
2022 Distinguished Bert O'Malley Endowed Lectureship, BCM, Houston, TX
2022 Kendall-Hench Lectureship in Endocrinology and Metabolism, Mayo Clinic, Rochester, MN
2022 John and Margaret Faulkner Lectureship, University of Michigan, MI
2021 Elected Member National Academy of Sciences (**NAS**)
2020 Senior Scholar Award - Global Consortium for Reproductive Longevity and Equality Found.
2020 Herzstein Endowed Professor in Molecular Physiology
2019 Elected Member American Academy of Arts and Sciences (**AAA&S**)
2019 42nd Steenbock Lectureship Award, U. of Wisconsin - Madison, WI
2018 Joseph Larner Memorial Lectureship Award in Pharmacology, U. of Virginia, VA
2018 Keynote Speaker - 8th Great Lakes Nuclear Receptors Conference, MN
2017 UCSF Chancellor's Martin Luther King, Jr. (MLK) Leadership Award
2012 Elected Fellow of the American Association for Advancement of Science (**AAAS**)
2011 Named NIH College of Reviewers
2009, 2011 Plenary Lectureships Endocrine Society
2008 American Diabetes Association Champion Gala Honoree
2006-Pres. Herzstein Distinguished Investigator in Molecular Physiology
2003 UCSF Outstanding Faculty Mentorship Award Nominee
2002 Brook Byers Basic Science Award
2001 Williams Lectureship for Pediatric Research

2000 First Named Lectureship for Women in the Society of Andrology
 1997-2002 NIH-Independent Scientist Development Award
 1991-1992 Genentech Human Growth Foundation Award
 1983-1984 W.M. Keck Foundation Fellow
 1982-1983 J. Aaron Charitable Foundation Fellow
 1981-1983 Muscular Dystrophy Fellowship

National Advisory Committees (Partial List)

2025 NIH Director's New Innovator Award Program (DP2) Editorial Board Reviewer
 2024 The Next Frontier in Women's Health Panelist, **The White House**, Washington, DC
 2024 Ad-Hoc NIH BNRS Review Panel
 2024 – Pres. Task Force for Scientific Advancement, American Physiological Society
 2023 – Pres. Scientific Advisor, Nutritional, Obesity Research Center, Baylor College of Medicine
 2023 – Pres. NASEM Committee on **Assessment of NIH Research on Women's Health**
 2023 – Pres. Scientific Advisory Board – K. Lisa Yang Brain-Body Center, MIT
 2022 Ad-Hoc NIH CSME Panel
 2021 Ad Hoc Inaugural NIH MPOD Panel, NINDS Blueprint for Neuroscience Panel
 2020 Ad Hoc Reviewer NIA – ERP Panel
 2019 ASBMR – Invited Contributor to Workshop on Aging – Sept 22, 2019
 2018 – Pres. Lead Organizer and Coordinator for UCSF Women in Discovery Science
 2018 – Pres. Organization for Study of Sex Differences, Elected Council Member
 2016 – 2020 Pennington NORC, Advisory Board Member
 2015 – 2020 **Chair**, NIDDK-B Review Panel, Permanent Member
 2015 – 2019 American Diabetes Association, Grant Review Panel Member
 2006 – 2019 Annual Review of Physiology-Endocrinology and Metabolism Section Editor
 2014 & 2018 Ad-Hoc Reviewer NIH IPOD Panel, NIDDK Program Project Review
 2014 Co-Chair, NIH Directors SEP – Illuminating the Druggable Genome
 2013 – 2016 American Heart Association Review Panel
 2012 – 2013 As Hoc NIH-NIDDK ZRG-SEP, ZEG-SEP, and ZDK1-SEP Panels
 2012 ADA Ad-Hoc Reviewer for Neurohormonal Control of Metabolism
 2011 **Chair**, NIH-NIDDK Program Project Review
 2011 NIDDK Stage 2 Editorial Board Review for R24 Collaborative Team Science
 2009 NIH Challenge Grants, Distinguished Editor for Physiological and Pathological Sciences
 2008 – 2009 NIH-NIDDK SEP Panels Feb 2008, Aug 2008, Feb 2009, March 2009
 2008 & 2009 **Co-Chair** American Heart Association Review Panel
 2008 **Chair**, SEP NIH Panel
 2006 **Chair**, Special Review Panel
 2004 – 2006 **Chair**, Molecular and Cellular Endocrinology NIH Study Section

C. Contributions to Science

1. Hormone Signaling in Sex-Specific Hypothalamic Function

My lab has defined important hormone-sensitive neuron clusters in the hypothalamus mediating sex-dependent metabolic and skeletal health relevant to female physiology.

- a. Cheung, C., Kurrasch, D.M., Liang, J., and **H.A. Ingraham**, Genetic Labeling Of SF-1 Neurons Reveals VMH Circuitry Beginning at Neurogenesis and The Emergence of a Separate Non-SF-1 Neuronal Cluster In The Ventrolateral VMH, [Journal of Comparative Neurology](#) (2013) Apr 15;521(6):1268-88. PMID: PMC4324838.
- b. Correa, SM, Newstrom, DW., Warne, JP., Cheung, C.C., Flandin, P., Pierce, AA., Xu, AW, Rubenstein, J.R. and **H.A. Ingraham**. An estrogen-responsive module in the ventromedial hypothalamus selectively drives sex-specific activity in females. [Cell Reports](#) (2016) Jan 6;10(1):62-74. Epub 2014 Dec 24. (2015) PMID: PMC4324838.
- c. Herber, CH, Krause, W.C., Wang, L-P., Bayrer, J.R., Li, A., Reid, MS, Fields, A., Hsiao, EC, Nomura, D., Nissenson, RA., Correa, SM and **H.A. Ingraham**, Estrogen signaling in arcuate Kiss1 neurons suppresses a sex-dependent female circuit promoting dense, strong bones, [Nat. Commun.](#) (2019). **10**: 163 PMID: 30635563 (BioRxiv 2018).
- d. Krause, W.C., R. Rodriguez, B. Gegenhuber, N. Matharu, A.N. Rodriguez, A.M. Padilla, K. Toma, C.B. Herber, S.M. Correa, X. Duan, N. Ahituv, J. Tollkuhn, and **H.A. Ingraham**,

Oestrogen engages brain MC4R signalling to drive physical activity in female mice. [Nature](#) (2021) Nov;599(7883):131-135. Epub 2021 Oct 13. PMID: 34646010. Highlighted in *NYT*, *Nature*, *Cell Metabolism*, and *Faculty Reviews*.

2. Structural Analyses of NR5A Nuclear Receptors (SF-1 and LRH-1)

In collaboration with the Fletterick lab, my lab led the initial efforts to understand how members of the NR5A family are ligand-activated. We showed that these receptors have large ligand-binding pockets and that the rodent LRH-1 is perfectly stable without ligands. However, we subsequently established that all other species of the NR5A subfamily could bind phospholipids, with the highest affinity ligands found to be the signaling phosphatidylinositols, PIP₂ and PIP₃.

- a. Krylova, I.N., Sablin, E.P., Moore, J., Xu, R.X., Waitt, G.M., MacKay, J.A., Juzumiene, D., Bynum, J.M., Madauss, K., Montana, V., Lebedeva, L., Suzawa, M., Williams, J.D., Williams, S.P., Guy, R.K., Thornton, J.W., Fletterick, R.J., Willson, T.M. and **H.A. Ingraham**, Structural analyses reveal phosphatidyl inositols (PI) as ligands for the NR5 orphan receptors SF-1 and LRH-1. [Cell](#) 120:343-355 (2005). PMID: 15707893
- b. Sablin, E., Krylova, I., Fletterick, R.J. and **H.A. Ingraham**, Structural basis for ligand-independent activation of the orphan nuclear receptor LRH-1. [Molecular Cell](#) 11:1575-1585 (2003). See Review "Activation Incarnate" by Martin L. Privalsky in *Developmental Cell* (2003). PMID: 12820970
- c. Sablin, E.P., Blind, R., Krylova, I.N., Ingraham, J.G., Cai, F., Williams, J.D., Fletterick, R.J., and **H.A. Ingraham**, Structure of SF-1 Bound by Different Phospholipids: Evidence for Regulatory Ligands. [Mol Endocrinology](#) 23(1):25-34 (2009). PMID: PMC2646595.
- d. Sablin EP, Blind RD, Uthayaruban R, Chiu HJ, Deacon AM, Das D, **Ingraham HA**, and Fletterick RJ. Structure of human LRH-1 LBD bound to the signaling phospholipid, PIP₃. [J Struct Biol](#). Sep 28. pii: S1047-8477(15)30067-8. (2015) PMID: PMC4651778.

3. Phospholipid Ligands for NR5A Nuclear Receptors

My lab has led efforts to define endogenous and synthetic ligands for the NR5A family. We have worked on developing assays to assess the effects of synthetic ligands on NR5A activity. Importantly, we were the first to discover that signaling lipids (PIP₂ and PIP₃) bind with high affinity to NR5A receptors. Later, we linked the production of diverse AA-phospholipid species to LRH-1 activity and hepatic lipid storage.

- a. Whitby, R.J., Stec, J., Blind, R.D., Dixon, S., Leesnitzer, L.M., Orband-Miller, L.A., Williams, S.P., Willson, T.M., Xu, R., Zuercher, W.J., Cai, F. and **H. A. Ingraham**, Small Molecule Agonists of the Orphan Nuclear Receptors Steroidogenic Factor-1 (SF-1, NR5A1) and Liver Receptor Homologue-1 (LRH-1, NR5A2). [Journal of Med Chem](#) 54(7):2266-81 (2011). PMID: PMC4151520.
- b. Blind, R.D., Suzawa, M. and **H.A. Ingraham**, Direct modification and regulation of the nuclear protein-lipid complex NR5A1-PIP₂ by the PI3-kinase IPMK. (**Cover and Podcast**) [Science Signaling](#) Jun 19;5(229) (2012) PMID: PMC3395721.
- c. Blind, R.D., Sablin, E.P., Kuchenbecker, K., Chui, H-J, Deacon, A., Das, D., Fletterick, R.J. and **H.A. Ingraham**, The Signaling Phospholipid PIP₃ Binds SF-1 Creating A New Interaction Surface at the Entrance of the Ligand Binding Pocket, [Proc Nat Acad Sci](#) Oct 21;111(42):15054-9 (2014) PMID: PMC4210282.
- d. Miranda, D.A., W.C. Krause, A. Cazenave, D.S. M. Suzawa, Escusa, Foo, J.C. Shihadih, A. Stahl, M. Fitch, E. Nyangau, M. Hellerstein, M.R. Wenk, D.L. Silver, and **H.A. Ingraham**. LRH-1 Regulates Hepatic Lipid Homeostasis and Maintains Arachidonoyl Phospholipid Pools Critical for Phospholipid Diversity, [JCI Insight](#) (2018) March 8th, Mar 8;3(5). pii: 96151. PMID:29515023.

4. Role of PTMs in Nuclear Receptor Activity and Tissue Development

My lab led efforts to understand the role of sumoylation on nuclear receptor activity. We were the first to establish that sumoylation modifies receptor activity and leads to the selective activation of SUMO-sensitive genes using both in vitro and in vivo data by knocking in a SUMO-less form of the receptor, which results in endocrine abnormalities and inappropriate steroid hormone production.

- a. Campbell, L.A., Faivre, E., Show, M.D., Ingraham, J.G., Flinders, J., Gross, J.D. and **H.A. Ingraham**, Decreased Recognition of SUMO-Sensitive Target Genes following Modification of SF-1 (NR5A1). [Mol Cell Bio](#) 28(24):7476-86 (2008). PMID: PMC2593425.

- b. Lee, F.Y., Faivre, E.J., Suzawa, M., Lontok, E., Ebert, D., Cai, F., Belsham, D.D. and **H.A. Ingraham**. Eliminating SF-1 (NR5A1) Sumoylation In Vivo Results in Ectopic Hedgehog Signaling and Disruption of Endocrine Development. (**Cover, Preview, and Podcast**), [Developmental Cell](#) 21:315-327 (2011), PMID: PMC3157481.
- c. Suzawa, M, Miranda, D.A., Ramos, K. A, Faivre, EJ, Ang, K.-H., Wilson, CG, Arkin, MR, Kim, Y-S., Diaz, A., Schneekloth, J.S. and **H. A. Ingraham**. Tannic Acid Identified in a Phenotypic Screen Inhibits Sumoylation and Activates SUMO-sensitive Transcriptional Programs In Vivo. [Elife](#). 2015 Dec 11;4. pii: e09003, PMID: PMC4749390, PMID: PMC5675444.
- d. Xing, Y, Zubir, M., Morohashi, K-H., **Ingraham, H.A.**, and G.D. Hammer. Timing of Adrenal Regression Controlled by Synergistic Interaction between Sf1 SUMOylation and Dax1, [Development](#) (2017) Oct 15;144(20):3798-3807, PMID:28893949.

5. Role of NR5A1 (SF-1) in Endocrine Tissue Development

My lab identified SF-1 as a major determinant of male sex differentiation by showing that this nuclear receptor regulates an essential peptide hormone (MIS, AMH) in the development of the bi-potential urogenital ridge. MIS leads to the destruction of the female reproductive tract in males. We went on to show that haploinsufficiency of SF-1 in mice leads to adrenal hypoplasia, similar to what has now been found in human heterozygous *SF-1* mutants.

- a. Shen, W-H., Moore, C.C.D., Ikeda, Y., Parker, K.L. and **H.A. Ingraham**, The orphan nuclear receptor, SF-1 regulates Müllerian inhibiting substance expression, a link in the sex determination pathway. [Cell](#) 77:651-661 (1994). PMID: 8205615
- b. **Ingraham, H.A.**, Lala, D., Ikeda, Y., Luo, X., Shen, W-H., Nachtigal, M., Abbud, R., Nilson, J.H., and K.L. Parker, The nuclear receptor steroidogenic factor 1 acts at multiple levels of the reproductive axis. [Genes & Development](#) (1994) 8:2302-2312. PMID: 7958897
- c. Nachtigal, M.W., Hirokawa, Y., VanHouten-Enyeart, D., Flanagan, J.N., Hammer, G.D. and **H.A. Ingraham**, Wilms' Tumor and Dax-1 modulate the orphan nuclear receptor, SF-1 in sex-specific gene expression. [Cell](#) 93:445-454 (1998). PMID: 9590178
- d. Bland, M.L., Jamieson, C., Akana, S., Bornstein, S.R., Eisenhofer, G., Dallman, M., and **H.A. Ingraham**, Haploinsufficiency of steroidogenic factor-1 in mice disrupts adrenal development leading to an impaired stress response. [Proc Nat Acad Sci](#) 97:14488-14493 (2000), PMID: PMC18946.

All Publications Link: <https://www.ncbi.nlm.nih.gov/myncbi/holly.ingraham.1/bibliography/public/>